

REMARKS

Claims 1-6, 8-17, and 19-36 are pending. Claims 19-36 have been withdrawn from examination as being drawn to nonelected subject matter. Claims 1-6 and 8-17 were rejected under 35 U.S.C. §112, first paragraph.

By this amendment, claims 13-16 have been canceled and claim 1 has been amended without prejudice or disclaimer of any previously claimed subject matter. Support for the amendments can be found, *inter alia*, throughout the specification including, for example, at page 2, lines 25-26, and at page 12, lines 2-3.

The amendments are made solely to promote prosecution without prejudice or disclaimer of any previously claimed subject matter. With respect to all amendments, Applicants have not dedicated or abandoned any unclaimed subject matter and moreover have not acquiesced to any rejections and/or objections made by the Patent Office. Applicants expressly reserve the right to pursue prosecution of any presently excluded subject matter or claim embodiments in one or more future continuation and/or divisional application(s).

Applicants have carefully considered the points raised in the Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejections Under 35 U.S.C. § 112, first paragraph

Claims 1-6 and 8-17 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The Examiner asserts that the specification "does not adequately teach a protocol, as claimed, that could be used to effect the required level of dopamine replenishment" and, in support

of this assertion, states that the “effect of dopamine replenishment is specific areas of the brain is unknown” and “the etiology of schizophrenia is not well-understood.” Office Action, page 3.

As herein amended, the claimed invention is directed to a method for providing dopamine or a dopamine precursor to a dopamine deficient prefrontal cortex of a subject with schizophrenia. In the claimed method, a cell/support complex comprising cells adhered to a support matrix is administered to the prefrontal cortex of the subject. The cells of the cell/support complex produce dopamine or a dopamine precursor.

Applicants respectfully submit that the specification provides all the required information for one of skill in the art to make and use the invention to provide dopamine or a dopamine precursor to the prefrontal cortex of a subject with schizophrenia. The specification teaches administration of the claimed cell/support complex to a prefrontal cortex of a patient with schizophrenia. The specification provides guidelines as to site and means of administration of the complex and guidance as to the number of cells which produce dopamine or a dopamine precursor to be administered to the patient. See, for example, page 12, lines 1-6, and page 22, line 19, to page 23, line 11. The specification teaches types of cells which produce dopamine or a dopamine precursor and types of support matrices appropriate for use in the claimed method. See, for example, pages 12-21. The specification teaches how to make the claimed cell support complex. See, for example, page 21, line 15, to page 22, line 6.

Accordingly, the specification teaches how to make and use the claimed invention without undue experimentation, i.e., the specification enables a method for providing dopamine or a dopamine precursor to a dopamine deficient prefrontal cortex of a subject.

Applicants respectfully submit that a *prima facie* case for lack of enablement has not been established.

While there may have been questioning regarding dopamine and schizophrenia in the art prior to the application filing date, it is now clear that dopamine deficits in particular brain areas

(e.g., prefrontal cortex) are associated with particular schizophrenia symptoms (e.g., negative symptoms). The Examiner, citing Seibyl et al. (U.S. Patent No. 5,447,948), points out that the art teaches that “mesofrontal dopamine deficits may be implicated in the negative symptoms of schizophrenia (Column 1, lines 44-57)” and that “the pathophysiology of schizophrenia includes both increased dopamine tone (in mesolimbic dopamine tracts) and decreased dopamine tone (in mesofrontal dopamine tracts).” Indeed, studies published since the filing of the application have served to support the association of these symptoms with regional dopamine deficits in the brains of schizophrenia patients.¹

Applicants respectfully submit that a well-understood etiology of schizophrenia is not required for enablement of the claimed invention, i.e., a method for providing dopamine or a dopamine precursor to a dopamine deficient prefrontal cortex of a subject with schizophrenia.

Applicants respectfully submit that the pending claims are in compliance with the enablement requirements.

Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 112, first paragraph.

CONCLUSION

Applicants believe that all issues raised in the Office Action have been properly addressed in this response. In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, reconsideration and allowance of the pending claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the Examiner is encouraged to contact Applicants' representative at the telephone number below.

¹ See, for example, Abi-Dargham et al. (2003) *The Neuroscientist* 9:404-416, enclosed herewith.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, Applicant(s) petition(s) for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or fees due in connection with this document to **Deposit Account No. 03-1952** referencing docket no. 311772000600.

Dated: December 31, 2003

Respectfully submitted,

By Karen R. Zachow

Karen R. Zachow, Ph.D.

Registration No.: 46,332

MORRISON & FOERSTER LLP

3811 Valley Centre, Suite 500

San Diego, California 92130

(858) 720-5191